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ETIOLOGICAL FACTORS AND PATHOGENETIC MECHANISMS OF SECONDARY DENTAL DEFORMATIONS: A SYSTEMATIC REVIEW

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Abstract

Background. Secondary dental deformations (SDD) develop as a result of complex interactions between local biomechanical triggers, inflammatory biological processes, and systemic modulating factors. Despite their high prevalence — affecting 40–65% of adult patients with partial edentulism — the etiological hierarchy and pathogenetic cascades underlying SDD remain incompletely characterized in an integrated framework. A systematic synthesis of available molecular, biomechanical, and epidemiological evidence is therefore needed.

Objectives. To systematically identify and critically evaluate the principal etiological factors contributing to SDD development; to characterize the pathogenetic mechanisms through which these factors produce morphological change at tissue, cellular, and molecular levels; and to quantify the relative contribution of each etiological category from available epidemiological data.

Methods. A systematic search of PubMed/MEDLINE, Scopus, Web of Science, and Cochrane Library (January 2000 – December 2024) was conducted according to PRISMA 2020 guidelines using terms including 'dental deformation etiology,' 'tooth migration mechanisms,' 'RANKL OPG dental,' 'periodontal biomechanics,' 'bruxism tooth displacement,' 'systemic disease tooth position,' and related MeSH headings. Of 1,612 records identified, 84 publications met inclusion criteria.

Results. Four principal etiological categories were identified: (1) tooth loss and absence of antagonist force (contributing to 35.2% of SDD cases); (2) periodontitis and alveolar bone destruction (22.1%); (3) parafunctional habits including bruxism (18.4%); and (4) orthodontic anomalies and relapse (14.8%). Systemic conditions — diabetes mellitus, osteoporosis, rheumatoid arthritis — act as amplifying cofactors rather than primary triggers, accelerating progression by 1.6–3.1-fold. The pathogenetic cascade operates through three converging mechanisms: biomechanical disruption of periodontal ligament force equilibrium, activation of the RANK/RANKL/OPG osteoclastic pathway, and inflammatory cytokine-mediated matrix degradation. Biomarker data from included studies document

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RANKL/OPG ratio elevations of up to 950% in active SDD compared to healthy controls.

Conclusions. SDD pathogenesis is multifactorial and dynamic. The RANK/RANKL/OPG axis is the central molecular pathway linking both mechanical and inflammatory etiological inputs to osteoclastic bone resorption and tooth displacement. Anti-inflammatory periodontal treatment must precede or accompany biomechanical correction to suppress the permissive inflammatory microenvironment that drives deformation relapse. Systemic disease management should be integrated into treatment planning as a determinant of force parameter selection and treatment timeline.

Keywords

secondary dental deformations; etiology; pathogenesis; RANKL; OPG; biomechanical mechanisms; periodontitis; bruxism; tooth migration; systemic cofactors

1. INTRODUCTION

Secondary dental deformations (SDD) are acquired positional changes in the dentition that arise in previously normal or functional dentitions as a consequence of identifiable etiological events. Unlike primary orthodontic malocclusions, which have a developmental basis, SDD are driven by ongoing biological processes that can in principle be interrupted or reversed if the etiological factors are identified and addressed. This therapeutic potential makes an accurate understanding of SDD etiology and pathogenesis directly relevant to clinical decision-making **[1, 2]**.

The study of SDD etiology has evolved considerably over the past three decades. Earlier literature focused almost exclusively on mechanical factors — tooth loss, parafunctional forces, and arch-length discrepancy — as primary drivers. The emergence of molecular biology in dental research during the 1990s and 2000s revealed that these mechanical inputs are transduced into tissue-level change through specific cellular and biochemical pathways, particularly the RANK/RANKL/OPG axis governing osteoclast differentiation and bone resorption **[3, 4]**. More recently, epidemiological studies have quantified the amplifying role of systemic conditions — most notably type 2 diabetes mellitus, osteoporosis, and autoimmune diseases — in accelerating deformation progression under otherwise equivalent mechanical loads **[5, 6]**.

Despite this accumulation of evidence, the etiological factors and pathogenetic mechanisms of SDD have not previously been synthesized in a single comprehensive, IMRAD-format review. This gap limits both clinical practice — where treatment planning is often guided by incomplete or empirical

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understanding of causal mechanisms — and research, where the absence of a shared etiological framework hampers cross-study comparison. The present systematic review is designed to address this gap.

2. METHODS

2.1. Search Strategy and Study Selection

The review was conducted and reported in accordance with PRISMA 2020 guidelines. Electronic databases searched included PubMed/MEDLINE, Scopus, Web of Science Core Collection, Cochrane Library, and EMBASE. The search period was January 1, 2000 to December 31, 2024. Search terms were developed iteratively and included: 'secondary dental deformation etiology,' 'dentoalveolar elongation mechanism,' 'tooth migration pathogenesis,' 'RANKL OPG periodontal ligament,' 'biomechanical tooth movement,' 'bruxism tooth displacement,' 'diabetes mellitus periodontal bone,' 'osteoporosis tooth mobility,' and related MeSH headings. No language restriction was applied at the search stage; non-English full texts were excluded at screening if no validated translation was available.

2.2. Inclusion and Exclusion Criteria

Studies were included if they: (1) enrolled human subjects or used validated in vitro/animal models relevant to human SDD; (2) reported data on etiological factors, cellular or molecular pathogenetic mechanisms, or systemic disease effects on tooth position or alveolar bone; and (3) used standardized definitions for SDD or closely related conditions (dentoalveolar elongation, mesial drift, tooth migration, occlusal collapse). Studies were excluded if they addressed primary orthodontic malocclusion only, reported case series of fewer than 20 subjects without mechanistic data, or lacked peer review.

2.3. Data Extraction and Quality Assessment

Two independent reviewers extracted the following data: study design, sample size, patient demographics, etiological factor studied, biological or mechanical outcome measures, biomarker levels with reference ranges, and statistical parameters. Discrepancies were resolved by consensus with a third reviewer. Quality of cohort and cross-sectional studies was assessed using the Newcastle-Ottawa Scale (NOS; maximum 9 stars). Quality of included systematic reviews and meta-analyses was assessed using AMSTAR-2. In vitro and animal studies were assessed using the SYRCLE risk-of-bias tool.

Table 1. Study Selection Summary (PRISMA 2020)

Stage	Records (n)	Excluded (n)
Initial database records identified	1,612	—
After duplicate removal	1,041	571

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Title and abstract screening	287	754
Full-text eligibility assessment	119	168
Studies included in final synthesis	**84**	35
of which: observational / cross-sectional	38	—
of which: cohort / longitudinal	22	—
of which: systematic reviews / meta-analyses	13	—
of which: RCTs and controlled clinical trials	8	—
of which: in vitro / animal mechanistic studies	3	—

Table 1. Study selection according to PRISMA 2020. RCT = randomized controlled trial.

3. RESULTS

3.1. Overview of Etiological Categories

Analysis of included studies identified four principal etiological categories that together account for the substantial majority of SDD cases, and a fifth category comprising systemic conditions that function as amplifying cofactors rather than primary triggers. Table 2 presents the pooled relative contribution of each primary category derived from six cross-sectional studies with standardized etiological classification (total n = 5,480) **[7–12]**.

Table 2. Relative Contribution of Primary Etiological Categories to SDD Development (Pooled, n = 5,480)

Etiological Category	n	Prevalence (%)	95% CI	Primary Mechanism
Tooth loss / absence of antagonist force	1,930	**35.2**	32.1–38.4	Elimination of occlusal counterforce; eruption potential released
Periodontitis / alveolar bone destruction	1,211	**22.1**	19.4–24.8	PDL attachment loss; RANKL-driven osteoclastic resorption
Parafunctional habits (bruxism, clenching)	1,008	**18.4**	15.8–21.0	Non-axial force overload; fatigue-type PDL damage
Orthodontic anomalies and relapse	811	**14.8**	12.4–17.2	Pre-existing arch

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				imbalance; post-treatment drift
Trauma and iatrogenic factors	274	**5.0**	3.6–6.4	Direct force application; bone architecture disruption
Congenital / developmental anomalies	246	**4.5**	3.1–5.9	Arch-length discrepancy; missing or supernumerary teeth
TOTAL	**5,480**	**100.0**	—	—

Table 2. PDL = periodontal ligament; RANKL = receptor activator of nuclear factor κB ligand. CI = confidence interval. Data pooled from [7–12].

3.2. Tooth Loss as the Primary Etiological Factor

Tooth loss is the dominant etiological trigger in SDD, implicated as the primary cause in 35.2% of cases. Its pathogenetic effect is exerted through three simultaneous mechanisms. First, extraction eliminates the occlusal antagonist force that normally restrains passive eruption of the opposing tooth, releasing its eruption potential. Second, the edentulous space created provides a path of least resistance into which adjacent teeth can drift mesially. Third, the alveolar bone resorption that follows extraction alters the biomechanical environment of neighboring teeth, reducing the lateral support that counters tipping forces **[13, 14]**.

The rate of secondary deformation following tooth loss is not uniform across time. A meta-analysis of 18 longitudinal studies by Tran et al. (2021) documented a mean supraalveolar elongation rate of 0.8–1.4 mm per year in the first 24 months after antagonist loss, accelerating to 2.1 mm per year (95% CI: 1.7–2.5 mm) in patients with concurrent periodontal disease **[15]**. Mesial drift of adjacent posterior teeth proceeds at a mean rate of 0.4 mm per year in the first year, increasing to 0.9 mm per year beyond three years if the extraction site remains unrestored, reflecting the progressive nature of force imbalance accumulation **[16]**.

Table 3. Mean Rates of Secondary Deformation Following Tooth Loss by Time Period and Periodontal Status

Deformation Type	**0–12 months (mm/yr)**	**12–36 months (mm/yr)**	**> 36 months (mm/yr)**	**Effect of Concurrent Periodontitis**
Supraalveolar elongation	0.8	1.2	0.5*	+160% increase (rate 2.1 mm/yr; 95% CI: 1.7–2.5)

				[15]
Mesial drift of adjacent teeth	0.4	0.7	0.9	+85% increase [16]
Transversal deviation	0.2	0.4	0.6	+40% increase [17]
Alveolar bone resorption at extraction site	1.1	0.6	0.3*	Not applicable; intrinsic to extraction sequela [18]

Table 3. *Rate decreases over time due to compensatory bone remodeling. Values represent mean mm/year of movement. Data from [15–18].

3.3. Periodontitis as an Etiological and Amplifying Factor

Chronic periodontitis contributes to SDD through direct destruction of the tooth's supporting apparatus. Loss of alveolar bone height, disruption of the principal periodontal ligament (PDL) fiber groups, and reduction in root attachment area collectively reduce the tooth's resistance to occlusal forces, enabling pathological displacement under loads that a healthy periodontium would tolerate without deformation **[19, 20]**.

The inflammatory cytokine environment of periodontitis directly activates osteoclastic bone resorption through upregulation of RANKL. Studies using immunohistochemical analysis of surgical specimens have demonstrated 3.8-fold higher osteoclast density in alveolar bone adjacent to periodontitis-affected teeth compared to healthy controls. This increase correlates significantly with the degree of tooth displacement ($r = 0.72$, $p < 0.001$), establishing a quantitative relationship between inflammatory burden and deformation magnitude **[21]**.

Periodontitis also amplifies SDD triggered by other primary causes. In patients with pre-existing periodontitis, the rate of supraalveolar elongation after antagonist loss is 160% higher than in periodontally healthy controls, the rate of mesial drift 85% higher, and the rate of transversal deviation 40% higher **[15, 16]**. This amplification effect indicates that periodontal status is not merely a concurrent finding in SDD patients but a biologically active modifier of the deformation process.

3.4. Parafunctional Habits

Bruxism, clenching, and other parafunctional habits contribute to SDD by generating occlusal forces that exceed the physiological adaptive capacity of the periodontium. Sleep bruxism generates peak bite forces of 400–900 N, compared to a normal masticatory force of 50–150 N, applied at non-functional directions and with prolonged duration extending up to several hours per night **[22]**. Piezoelectric tooth monitoring in patients with polysomnographically confirmed sleep bruxism has demonstrated cumulative daily force exposure 8-fold higher than in non-

bruxist controls, with force vectors deviating from the tooth's long axis by 15–30° **[23]**.

The pathogenetic effect of parafunctional forces operates through the same RANKL-mediated pathway as periodontitis, but the initiating stimulus is mechanical rather than microbial. Excessive non-axial force creates differential compression and tension zones within the PDL; the compression zone suppresses osteoblastic activity while simultaneously upregulating RANKL expression in PDL fibroblasts, driving osteoclast differentiation and net bone resorption on the pressure side, which results in progressive tooth displacement toward the area of reduced mechanical resistance **[24]**.

3.5. Orthodontic Anomalies and Post-Treatment Relapse

Pre-existing orthodontic anomalies predispose to SDD by creating arch-length discrepancies, altered occlusal contact patterns, and abnormal force vector distributions that make the dentition inherently less stable. Post-orthodontic relapse — estimated to affect 20–40% of patients without adequate retention — produces secondary deformations that combine features of the original malocclusion with newly acquired displacement patterns **[25, 26]**. The etiological role of orthodontic anomalies is therefore dual: direct production of SDD through arch instability, and indirect amplification of SDD triggered by superimposed tooth loss or periodontitis acting on a structurally compromised dentition.

3.6. Pathogenetic Mechanisms

3.6.1. Biomechanical Pathway

The biomechanical pathway is initiated by disruption of occlusal force equilibrium. In a healthy dentition, each tooth is maintained in position by a balance of forces: mesial drift tendency is counteracted by interdental contacts; eruption tendency is balanced by antagonistic occlusal forces; and axial forces are directed along the tooth's long axis, ensuring uniform PDL loading. When this equilibrium is disrupted — by tooth loss, parafunctional habits, or traumatic occlusion — force vectors become non-axial **[27]**.

Non-axial forces produce differential compression and tension zones within the PDL. The Schwarz pressure-tension theory, validated by subsequent biomechanical finite element analysis studies, posits that compression zones stimulate osteoclastic resorption while tension zones promote osteoblastic deposition, resulting in net tooth movement toward the area of reduced resistance **[28]**. Finite element models of the human periodontium confirm that even a 10° deviation from the axial force vector produces PDL stress concentrations of 2.3–3.8 MPa — values that exceed the theoretical threshold for osteoclast activation (approximately 1.5 MPa) — at the cervical and apical root regions **[29]**.

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Table 4. Biomechanical Parameters of Tooth Displacement — Finite Element Analysis Data

Parameter	Physiological Range	SDD Threshold	SDD Active Phase	Reference
Peak PDL compressive stress (MPa)	0.3–1.2	~1.5	2.3–4.8	[29, 30]
Force vector deviation from long axis (°)	0–5°	~10°	15–35°	[28]
Masticatory force magnitude (N)	50–150	> 200	250–900*	[22]
Daily non-axial force exposure duration (min)	< 20	> 40	80–420*	[23]
Osteoclast density (cells/mm² alveolar bone)	2.1 ± 0.8	—	8.0 ± 2.3	[21]
Alveolar bone resorption rate (mm/yr)	< 0.1	0.2	0.6–2.1	[15]

Table 4. *Values from bruxism patients with confirmed sleep bruxism (polysomnography). PDL = periodontal ligament. Data from [15, 21–23, 28–30].

3.6.2. Molecular and Cellular Mechanisms — RANK/RANKL/OPG Pathway

At the molecular level, the RANK/RANKL/OPG axis is the central regulatory pathway governing bone turnover in SDD pathogenesis. RANKL (receptor activator of nuclear factor κB ligand), expressed by PDL fibroblasts and osteoblasts under both mechanical stress and inflammatory cytokine stimulation, binds to the RANK receptor on osteoclast precursor cells, driving their differentiation and activation into mature bone-resorbing osteoclasts. Osteoprotegerin (OPG), a decoy receptor that competitively inhibits RANKL binding to RANK, is the primary brake on osteoclastic activity; its downregulation by inflammatory cytokines (TNF-α, IL-1β) and mechanical overloading releases this brake and results in net bone resorption **[31, 32]**.

Both principal etiological inputs — mechanical force overload and periodontal inflammation — converge on this same molecular pathway through distinct upstream signals. Mechanical overload activates the Wnt/β-catenin and NF-κB signaling pathways in PDL fibroblasts, upregulating RANKL gene expression and downregulating OPG. Bacterial lipopolysaccharides and the inflammatory milieu of periodontitis activate Toll-like receptors and NF-κB independently, producing an additive or synergistic effect on RANKL/OPG imbalance in teeth affected by both etiological inputs simultaneously **[33, 34]**.

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Table 5. Molecular Biomarker Levels in Gingival Crevicular Fluid: Healthy Controls vs. Active SDD

Biomarker	Healthy Controls (mean ± SD)	Active SDD (mean ± SD)	Change (%)	p-value	Reference
RANKL (pg/mL)	12.4 ± 3.2	47.8 ± 9.1	**+285**	< 0.001	[32]
OPG (pg/mL)	38.5 ± 7.4	14.2 ± 4.8	**−63**	< 0.001	[33]
RANKL/OPG ratio	0.32	3.36	**+950**	< 0.001	[33]
IL-1β (pg/mL)	2.1 ± 0.9	18.7 ± 5.2	**+790**	< 0.001	[34]
TNF-α (pg/mL)	1.4 ± 0.6	12.3 ± 3.8	**+778**	< 0.001	[35]
PGE_2 (ng/mL)	0.8 ± 0.3	4.7 ± 1.1	**+488**	< 0.001	[36]
MMP-8 (ng/mL)	14.2 ± 4.6	52.9 ± 14.7	**+273**	< 0.001	[37]
Sclerostin (pg/mL)	44.1 ± 9.8	71.6 ± 18.3	**+62**	0.003	[38]

Table 5. GCF = gingival crevicular fluid; MMP-8 = matrix metalloproteinase-8; PGE_2 = prostaglandin E_2; OPG = osteoprotegerin; RANKL = receptor activator of nuclear factor κB ligand; SD = standard deviation. All measurements from GCF sampled with standardized Periopaper strips.

3.6.3. Inflammatory Cytokine Cascade

The inflammatory cytokine cascade in SDD operates in close coordination with the RANKL/OPG axis. IL-1β is the most potent osteoclastogenic cytokine in the periodontal environment, stimulating RANKL expression in osteoblasts and PDL fibroblasts while simultaneously suppressing OPG production. Its mean concentration in GCF samples from teeth with active SDD (18.7 ± 5.2 pg/mL) is 790% above healthy control levels, as shown in Table 5. TNF-α acts synergistically with IL-1β, directly activating NF-κB in osteoclast precursors independently of RANKL, providing a RANKL-independent amplification loop that maintains osteoclast activity even when RANKL signaling is partially blocked **[35, 39]**.

Matrix metalloproteinases (MMPs), particularly MMP-8 (collagenase-2), are responsible for extracellular matrix degradation in the periodontal ligament during active SDD. The 273% elevation of MMP-8 in GCF from SDD-affected sites reflects ongoing collagen fiber breakdown that reduces the structural integrity of the PDL attachment apparatus, facilitating progressive tooth displacement **[37]**. Prostaglandin E_2 (PGE_2) contributes by stimulating cAMP-mediated RANKL upregulation in osteoblasts and by directly promoting osteoclast bone-resorbing activity; its 488% elevation in active SDD GCF indicates a significant prostaglandin-mediated component to the osteoclastic activation observed **[36]**.

3.6.4. Integrated Pathogenetic Cascade

The convergence of biomechanical and inflammatory inputs on the RANKL/OPG axis means that the overall pathogenetic cascade can be summarized

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as a sequential process, illustrated schematically in Table 6. Understanding this cascade has direct therapeutic implications: interventions must target the appropriate stage of the cascade to be effective. Prosthetic correction alone does not address the inflammatory microenvironment that drives relapse; conversely, anti-inflammatory periodontal therapy without biomechanical rehabilitation does not restore force equilibrium and will not prevent progressive deformation.

Table 6. Integrated Pathogenetic Cascade of Secondary Dental Deformations — Step-by-Step Summary

Step	Event	Biological Mechanism	Clinical Correlate
1	Primary etiological er	Tooth extraction eliminates gonist force; bacterial biofilm ates PDL inflammatory nse; parafunctional forces rate non-axial PDL stress	History of extraction, dontitis diagnosis, or sm; identifiable at patient ry stage
2	Disruption of sal force equilibrium	Eruption potential strained; force vectors deviate tooth long axis; asymmetric loading zones created	Absence of occlusal contact; ature contacts; deflective rsion paths on occlusal sis
3	PDL mechanical l transduction	Compression zones activate β-catenin and NF-κB in PDL blasts; tension zones promote blastic activity; differential -specific response initiated	Not directly visible ally; detectable as PDL ning on CBCT in early stages
4	RANKL upregulation G downregulation	PDL fibroblasts and blasts express increased KL; inflammatory cytokines β, TNF-α) suppress OPG; KL/OPG ratio rises up to above normal	Elevated GCF biomarkers table by ELISA; not routinely ured in clinical practice but ant in research
5	Osteoclast rentiation and ation	RANKL binds RANK on clast precursors; mature clasts form and secrete H^+ and cathepsins; bone mineral lved; organic matrix aded by MMP-8	Alveolar bone loss visible on pical radiograph; angular defects; crest height ction
6	Tooth displacement	Bone resorption on pressure removes structural resistance; moves toward resorption ; carried alveolar bone may rtrophy on tension side e IB)	Clinically measurable crown ion change; tipping angle on graph; occlusal contact bution altered on T-Scan
7	Secondary force	Displaced tooth creates new	Progressive multi-tooth

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	lance	sal interferences; adjacent opposing teeth experience ed force vectors; cascade agates to neighboring units	vement; deepening occlusal mpensation stage (Okeson I → II → III)
8	Established SDD self-sustaining gy	Chronic inflammatory environment maintains KL elevation; mechanical rmation amplifies biological ity; positive feedback loop lished	Complete clinical SDD nosis; TMJ involvement in III; functional mpensation requiring disciplinary management

Table 6. PDL = periodontal ligament; RANKL = receptor activator of nuclear factor κB ligand; OPG = osteoprotegerin; CBCT = cone-beam computed tomography; GCF = gingival crevicular fluid; TMJ = temporomandibular joint; ELISA = enzyme-linked immunosorbent assay.

3.7. Systemic Cofactors

Systemic conditions do not directly initiate SDD in the absence of a local primary trigger, but they substantially accelerate progression and reduce the effectiveness of compensatory bone remodeling. Table 7 summarizes the principal systemic cofactors identified in the included literature with their mechanisms and quantified effects on SDD risk.

Table 7. Systemic Conditions as Amplifying Cofactors in SDD Progression

Systemic Condition	Mechanism of Amplification	Risk Modification	Evidence Level	Reference
Type 2 Diabetes Mellitus	Reduced osteoblast function via AGE-RAGE pathway; impaired neutrophil chemotaxis; elevated systemic IL-6 and TNF-α	**2.4× increased risk**	Level Ib (RCT)	[40]
Post-menopausal Osteoporosis	Reduced BMD; estrogen deficiency removes inhibitory effect on osteoclast differentiation; impaired PDL mechanical support	**1.9× increased drift rate**	Level IIa (cohort)	[41]

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Rheumatoid Arthritis	Systemic elevation of TNF-α, IL-6, and IL-17; generalized osteoclastic activation; direct TMJ involvement	**3.1× increased alveolar bone loss rate**	Level Ib	[42]
Vitamin D Deficiency (< 20 ng/mL)	Impaired calcium-phosphate mineralization; PDL fiber mechanical properties reduced; osteoblast suppression	**1.7× increased SDD risk**	Level IIb	[43]
Hypothyroidism	Slowed bone turnover; delayed PDL remodeling; altered healing response to mechanical loading	**1.6× slower but irreversible deformation**	Level IIb	[44]
Smoking (> 10 pack-years)	Vasoconstriction of PDL microvasculature; impaired neutrophil function; increased matrix metalloproteinase expression	**1.8× accelerated progression**	Level Ib	[45]
Long-term Bisphosphonate Therapy	Suppression of osteoclast differentiation and apoptosis; reduced bone resorption rate (protective effect)	**−42% reduction in drift rate**	Level IIa	[46]

Table 7. AGE-RAGE = advanced glycation end-products receptor pathway; BMD = bone mineral density; PDL = periodontal ligament; TMJ = temporomandibular joint. Evidence levels per Oxford Centre for Evidence-Based Medicine 2011 [47].

3.8. Age and Gender Effects on Etiological Pathways

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Age and gender influence SDD progression primarily by modulating bone metabolism rather than by changing the etiological triggers themselves. Younger patients (18–35 years) exhibit faster initial tooth movement due to higher bone turnover rates and greater PDL cellular responsiveness; however, their deformations also show greater spontaneous compensation and are more amenable to orthodontic correction **[48]**. Older patients (> 55 years) demonstrate reduced bone formation capacity, meaning that osteoclast-driven resorption is less effectively counterbalanced by opposing osteoblastic deposition; as a result, equivalent etiological stimuli produce more severe and less reversible deformations **[49]**.

Gender differences in SDD progression are mediated primarily through the effects of sex hormones on bone metabolism. Estrogen inhibits osteoclast differentiation and promotes OPG expression; estrogen deficiency in post-menopausal women removes this inhibitory effect, producing a systemic increase in RANKL/OPG ratio that augments the local pro-resorptive environment at SDD-affected sites. A cross-sectional study of 1,240 patients found that each decade of age in women was associated with a 0.4 mm increase in mean supraalveolar deformation magnitude after controlling for duration of tooth loss (β = 0.42; 95% CI: 0.38–0.46; $p < 0.001$), a relationship not observed in men after adjustment for the same covariates **[50]**.

Table 8. Influence of Age and Gender on SDD Progression Rate (Pooled Analysis, n = 3,420)

Age Group	n	Overall Prev. (%)	Male (%)	Female (%)	Dominant SDD Type	p (sex diff.)
18–34 years	520	14.2	12.8	15.6	Mesial drift	0.214
35–44 years	780	38.7	35.4	41.9	Supraalveolar IA	0.032*
45–54 years	890	**54.3**	49.2	59.1	Supraalveolar IB	0.018*
55–64 years	730	**61.8**	58.4	65.2	Combined type	0.041*
≥ 65 years	500	58.4	55.1	61.7	Combined type	0.099

Table 8. *Statistically significant sex difference ($p < 0.05$). Data pooled from [49, 50].

4. DISCUSSION

This systematic review of 84 peer-reviewed publications provides an integrated analysis of SDD etiology and pathogenesis that has several important clinical and research implications.

The most significant finding is the convergence of all major etiological inputs — mechanical force imbalance, periodontal inflammation, and parafunctional overload — on the same molecular pathway: the RANK/RANKL/OPG axis. The 950% elevation of RANKL/OPG ratio in GCF from teeth with active SDD, derived from data pooled across multiple independent studies using standardized sampling protocols, represents a remarkably consistent biological signature of the condition. This convergence has a direct therapeutic implication that is not always reflected in current clinical guidelines: treatment of SDD cannot be confined to biomechanical correction alone. Because the RANKL-mediated inflammatory microenvironment maintains osteoclastic activity independently of the original mechanical trigger, prosthetic rehabilitation without concurrent periodontal anti-inflammatory treatment creates conditions for biological relapse even when the mechanical cause has been eliminated **[33, 34]**.

The second important finding is the quantified amplification effect of systemic conditions. The 2.4-fold increase in SDD risk in type 2 diabetes patients and the 3.1-fold increase in alveolar bone loss rate in rheumatoid arthritis patients are not marginal effects; they represent a clinically meaningful difference in prognosis that should influence treatment planning. Current prosthetic rehabilitation protocols are largely calibrated for metabolically healthy patients. In systemically compromised patients, the same prosthetic force parameters produce substantially greater biological responses, necessitating modified biomechanical designs, extended treatment timelines, and closer monitoring intervals. The evidence reviewed here supports a multidisciplinary approach in which systemic disease management is explicitly integrated as a determinant of prosthetic treatment parameters, rather than treated as an independent medical co-morbidity **[40, 41, 42]**.

Third, the age and gender data in Table 8 highlight the post-menopausal period as a particularly high-risk window for SDD initiation and acceleration. The significantly higher rates of supraalveolar elongation Type IB — the most surgically demanding subtype — in women aged 45–64 years, combined with the known estrogen-mediated mechanism, indicate that this population should be targeted for preventive prosthetic rehabilitation with greater urgency than current practice guidelines typically specify. The identification of hormonal status as a modifiable cofactor also raises the question of whether systemic hormone replacement therapy or selective estrogen receptor modulators could be considered as adjuncts to SDD

prevention in selected post-menopausal patients with high tooth-loss risk, a research question not yet addressed in controlled clinical trials.

The main limitation of this review is the heterogeneity of biomarker measurement methodologies across included studies. GCF RANKL and OPG measurements are highly sensitive to sampling technique, storage conditions, and assay platform; direct numerical comparison across studies from different centers therefore carries uncertainty despite the use of standardized mean-difference calculations. Future research should prioritize multicenter studies with harmonized biomarker protocols to enable more precise quantification of the RANKL/OPG signal in SDD.

5. CONCLUSIONS

Secondary dental deformations are multifactorial conditions driven by the convergence of mechanical, biological, genetic, and systemic inputs. Tooth loss is the dominant primary etiological trigger (35.2% of cases), operating through elimination of antagonist balance, creation of drift space, and post-extraction alveolar remodeling. Periodontitis amplifies progression through RANKL-driven osteoclastic activation, increasing deformation rates by 85–160% compared to periodontally healthy controls.

The central pathogenetic pathway is the RANK/RANKL/OPG axis, which receives convergent inputs from both mechanical (PDL stress transduction via Wnt/NF-κB) and inflammatory (cytokine-mediated NF-κB activation) etiological sources. The 950% elevation of RANKL/OPG ratio in GCF from active SDD sites, alongside 778–790% increases in TNF-α and IL-1β, constitutes a quantifiable molecular signature of the condition that warrants integration into diagnostic and treatment-response monitoring protocols.

Systemic conditions — particularly type 2 diabetes (2.4× risk), rheumatoid arthritis (3.1× alveolar bone loss), and post-menopausal estrogen deficiency — function as amplifying cofactors that substantially accelerate progression and must be addressed in treatment planning. Anti-inflammatory periodontal therapy must be sequenced before or concurrently with biomechanical prosthetic correction to suppress the self-sustaining inflammatory microenvironment that drives relapse. A multidisciplinary management model integrating periodontology, prosthetics, and internal medicine is the evidence-based standard for patients with systemic cofactors.

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